The new and non-transparent Cancer Drugs Fund

Wood, Eifiona; Hughes, Dyfrig

PharmacoEconomics

DOI:
10.1007/s40273-019-00871-9

Published: 01/01/2020

Peer reviewed version

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Authors: Eifiona M Wood, Dyfrig A Hughes

Affiliation: Centre for Health Economics and Medicines Evaluation, Bangor University, UK

Correspondence to:

Dyfrig Hughes

Centre for Health Economics and Medicines Evaluation

Bangor University

Ardudwy, Holyhead Road

Bangor

LL57 2PZ

Telephone: 01248 382950

E-mail: d.a.hughes@bangor.ac.uk

Word count: 1458

References: 18

Contributions

Eifiona Wood and Dyfrig Hughes made substantial contributions to the conception and design of the work; the acquisition, analysis, and interpretation of data; drafted the work and revised it critically for important intellectual content; approved the version to be published; and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding

Dyfrig Hughes is a Health and Care Research Wales Senior Research Leader.

Compliance with Ethical Standards

Conflict of Interest

Eifiona Wood and Dyfrig Hughes declare they have no conflicts of interest.

Introduction

The Cancer Drugs Fund (CDF) in England was established in 2011 to facilitate access to cancer medicines that were not routinely available on the National Health Service (NHS). By 2015/16, the cost of the CDF had reached £1.27bn[1], and its value has been criticised extensively[2–4] . Since July 2016, a new arrangement which involves the National Institute for Health and Care Excellence (NICE) in the appraisal of CDF medicines came into effect[5]. Medicines on the CDF as of 31st March 2016 were appraised by NICE and their continued funding was dependent on an expenditure control mechanism to prevent overspend as had happened in previous years (e.g. by £126m (37%) in 2015/16). Under the current scheme, new cancer medicines may be recommended by NICE for routine commissioning (if considered to be clinically and cost-effective), recommended for use within the new CDF (if there is good potential, but considerable clinical uncertainty) or not recommended at all. Medicines available via the new CDF require a Managed Access Agreement, which consists of a Data Collection Arrangement, setting out which data are to be collected to resolve clinical uncertainty, and a Commercial Agreement that determines how much the NHS will pay for the treatment during the managed access period.

Since April 2016 and the introduction of the new CDF, NICE has accelerated its review of cancer medicines listed on the original CDF, as well as newer cancer medicines. During the two year period to March 2018, 40 cancer treatments for 54 indications were recommended for routine commissioning by NICE[6]. Medicines for 34 of these indications were considered under the NICE End of Life policy [7], which places a maximum weighting of 2.5 on quality-adjusted life year (QALY) gains. This, in effect, increases the cost effectiveness threshold from the £20,000 to £30,000 range, to £50,000 per QALY.

There is a concerning trend in the lack of transparency in relation to CDF medicines; specifically, as explored in this commentary, in respect to their value and overall cost to the NHS. This is further exacerbated by medicines remaining on the CDF beyond specified time-limited periods.

Value of CDF medicines

There is very limited public disclosure of the value of new cancer medicines. Following the introduction of the new CDF and resultant stricter inclusion criteria, as well as a drive by NICE to clear the backlog of medicines that were within the CDF without review, a NICE recommendation or inclusion within the CDF has required that medicines fall within accepted cost-effectiveness thresholds. Companies have achieved the requisite reduction in ICERs through offering confidential discounts to listed drug prices. While NICE aims to ensure that its appraisal processes are as transparent as possible, the

widespread use of “commercial-in-confidence” pricing discounts agreed between NHS England and the manufacturer prevents independent scrutiny of the decision-making process.

In the 2-year period from April 2016, justifications provided by NICE for the positive recommendation of 36 of 70 treatment comparisons involving routinely commissioned CDF medicines, were on the basis of them being a “cost-effective use of NHS resources” or falling “below the NICE threshold” or were not even clearly defined (Table 1). Fifty one percent of comparisons lacked transparency to the extent that the ICERs used for decision-making were not reported.

Over the same period, NICE appraised 27 CDF medicines for 42 clinical indications involving 48 treatment comparisons. Nearly a half (20/42) were legacy indications from the original CDF and a third (14/42) were appraised using the end of life criteria. The reporting of decision-making ICERs is even more notably absent, with ICER values reported for only 6 of the 48 comparisons, (avelumab TA517, brentuximab TA446, ibrutinib TA502, ixazomib TA505, nivolumab TA483 and nivolumab TA490) with a further 2 comparisons reported as being dominant (lenvatinib with everolimus TA498). The large majority (83%) of comparisons failed to report any decision-making values, but rather, used generic statements such as being “within acceptable NICE thresholds”, or with “plausible potential to be cost-effective” or, in 16/42 cases, were without a published technology appraisal.

Decisions were not routinely bound by NICE cost-effectiveness thresholds. For all reviewed treatments in routine commissioning and funded within the CDF, 7 interventions, which considered 9 comparisons, were approved for funding when the ICERs were subject to multiple scenarios and were reported as a range which crossed thresholds, or were above the NICE thresholds (abiraterone TA387, enzalutamide TA377, ponatinib TA451, ixazomib TA505, lenvatinib ID1059, nivolumab TA483, sorafenib ID1059). In the case of lenvatininb and sorafenib for the treatment of differentiated thyroid cancer after radioactive iodine, both were recommended with unspecified ICERs in excess of £30,000 per QALY on the basis of uncaptured benefits and there being no other treatment option for a rare disease, despite rarity in general not justifying a higher threshold[8].

Despite NICE stating that “Data that are likely to be fundamental to the appraisal committee's decision-making cannot be marked as confidential (for example, the incremental cost-effectiveness ratio estimates)”[9], access to this information is inconsistent through the use of variable redaction practices[10] to protect undisclosed price discounts. As a consequence, neither NHS hospital managers and commissioners responsible for allocating funds and delivering treatment, nor the tax-paying general public who fund healthcare in England and Wales are informed of the true value of these new cancer treatments. It is clear that primacy is given to protecting commercial confidentiality, which is especially important to the pharmaceutical industry given that UK drug prices are widely referenced

by other countries and a reported ICER value could be used to back-calculate the NHS-agreed price. However, this price concealment may soon no longer be acceptable, as the World Health Assembly resolution to publicly disclose medicine prices gains momentum, despite reservations by the UK[11].

Unknown cost

It is equally difficult to determine the overall cost of CDF treatments. NHS England reported that in 2017-18, the CDF operated within its capped funding allowance of £340m, with a total spend of just over £200m[12], the underspend associated with a high number of medicines shifting out of the CDF and into routine commissioning following NICE appraisal during this time period. NHS England expenditure on the 40 cancer treatments that transitioned from the CDF to routine commissioning between April 2016 and March 2018 increased from £686 million in 2015/16 to over £1,100 million in 2017/18[13], with the top 10 medicines by increase in spend (cabozantinib, dabrafenib, enzalutamide, ibrutinib, nivolumab, palbociclib, pembrolizumab, pertuzumab, ruxolitinib and trametinib) accounting for over 90% of the increase overall. Expenditure on pembrolizumab alone increased from £12m to £142m during this period, a considerable cost for a medicine of (publicly) unknown value[14].

Time on CDF

Transparency is not only lacking for cost-effectiveness data, but also for time within the CDF. NHS England's new CDF Standard Operating Procedure specifies that drugs should be funded through the CDF for a time period that is to be as short as possible[5]. This is usually, but not exclusively, two years, whilst allowing for some flexibility in relation to uncertainty, the rarity of the cancer and the source of the data which addresses the uncertainty[15]. However, this time limit is not consistently adhered in practice. By March 2018, the two year window was met by only 14 (33%) of the 42 indications in the new CDF (Table 2), with 3 (7%) being, or expected to be, funded within the CDF for between 3-4 years, and 6 (14%) for more than 4 years. The expected duration of time in the CDF was unknown for a further 14 (33%) indications, with the majority of these either suspended, or with no data to suggest how long CDF funding will continue, or any justification for either their original or ongoing inclusion with the fund.

Implications

NICE considers interventions with ICERs below £20,000 per QALY to generally be a cost-effective use of NHS resources[16]. This threshold is increased to £30,000 per QALY for interventions considered innovative, or if there are particular features relevant to the condition or population receiving the medicines, or potential for a broader societal impact. Medicines which are recommended at these values may in fact reduce population health based on the Department of Health and Social Services'

use of £15,000 per QALY as an estimate of the health opportunity cost of NHS expenditures[17]. The approval of medicines that qualify for appraisal under the life-extending, end of life criteria further impact on population health[18]. The uncertainty, through lack of transparency, of the potential health opportunity cost of NICE-approved cancer medicines poses a risk, both to the integrity of NICE in upholding one of its key procedural principles to provide services in a fair and appropriate manner[8], and NHS constitutional commitments to maximise benefits from NHS resources[19]. In making decisions implicit, transparency is disputed, and opportunities for independent examination denied in assessing the value of NHS treatments.

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Table 1: Reporting of the ICERs of cancer treatments recommended by NICE for routine commissioning, and for new CDF treatments, between April 2016 and March 2018

	Reported values of ICER range or dominance				No ICER value reported by rationale for recommendation					
	ICER below threshold, or dominant		ICER crosses or above thresholds		Below threshold		Not defined		No technology appraisal	
Threshold for decision-making	**Routine commissioning**	**New CDF**	**Routine commissioning**	**New CDF**	**Routine commissioning**	**New CDF**	**Routine commissioning**	**New CDF**	**Routine commissioning**	**New CDF**
Cost minimisation with equivalent health outcomes	-	-	-	-	1	-	-	-	-	-
≤£30k per QALY	15	2	5	1	14	8	3	5	-	-
£30k to £50k per QALY (meeting "end of life" criteria)	14	4	-	1	18	1	-	10	-	-
Unknown	-	-	-	-	-	-	-	-	-	16
Total (% of routine commissioning or new CDF)	29 (41%)	6 (13%)	5 (7%)	2 (4%)	33 (47%)	9 (19%)	3 (4%)	15 (31%)	0 (0%)	16 (33%)

[a]All data are based on NICE technology appraisal reports for interventions listed in the National Institute for Health and Care Excellence and NHS England, National Cancer Drugs Fund List ver1.72 28-Mar-18

Table 2: Time spent in CDF, all drug indications, April 2016 to March 2018 (N=42)

	Time in CDF[a]				
CDF status	**≤ 2 years**	**2 - 3 years**	**3 - 4 years**	**≥ 4 years**	**Unknown**
Managed Access Scheme	3	5	3	5	
Technology appraisal in progress	5				1
Transition to routine funding	5				
Suspended					2
Discontinued	1				1
No data				1	10
Total, n (%)	14 (33%)	5 (12%)	3 (7%)	6 (14%)	14 (33%)

[a] All data are based on NICE technology appraisal and Managed Access Agreement (MAA) reports for interventions listed in the National Institute for Health and Care Excellence and NHS England, National Cancer Drugs Fund List ver1.72 28-Mar-18. Time in CDF was calculated from the entry date into new CDF to the estimated date of NICE guidance publication. Where no date of publication was available, an estimated date was assumed, based on the MAA reported end of data collection date, plus 90 days clinical analysis, 90 days submission preparation and 230 days NICE review. Some MAAs indicate 4 months to submission post clinical data ready, suggesting 90 days for submission is conservative.